INPLASY

SGLT-2 Inhibitors Across the Complete Spectrum of Chronic Kidney Disease Aetiology: A Meta-Analysis of 21 Trials and 78,614 Participants Through May 2026

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ADMINISTRATIVE INFORMATION

Support - Self-funded. University of Hail College of Pharmacy academic resources. No pharmaceutical industry or commercial funding received.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202660013

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 June 2026 and was last updated on 2 June 2026.

INTRODUCTION

Review question / Objective Is SGLT-2 inhibitor renoprotection consistent across the full CKD aetiology spectrum regardless of diabetes status, albuminuria level, or nephropathy type, and is the benefit durable at 5 years?

Rationale This systematic review addresses a critical evidence gap. No comprehensive synthesis with pre-specified interaction analyses currently exists for this topic. Prospective registration ensures transparency and minimises reporting bias.

Condition being studied Chronic kidney disease of any aetiology, with or without type 2 diabetes.

METHODS

Search strategy PubMed/MEDLINE, Embase, Cochrane CENTRAL, and Scopus from January 1, 2000 to May 31, 2026. ClinicalTrials.gov and WHO-ICTRP on May 31, 2026. Key terms: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, SGLT-2 inhibitor, chronic kidney disease, CKD, nephropathy, eGFR, proteinuria, IgA nephropathy, DAPA-CKD, EMPA-KIDNEY, CREDENCE, PROTECT, SMART-C.

Participant or population Adults aged 18 or above with confirmed CKD (eGFR below 60 mL/min/1.73m2, UACR above 30 mg/g, or both).

Intervention Any SGLT-2 inhibitor (empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin) at any approved or investigational dose.

Comparator Placebo or active comparator without SGLT-2 inhibitor activity, on background standard of care including maximum-tolerated RAAS blockade.

Study designs to be included Placebo-controlled or active-comparator RCTs of SGLT-2 inhibitors in adults with confirmed CKD, reporting at least one pre-specified renal or cardiovascular endpoint. Pre-specified subgroup analyses from eligible trials incorporated as separate data sources.

Eligibility criteria Inclusion: Adults with CKD (eGFR below 60, UACR above 30 mg/g, or both); any SGLT-2 inhibitor at any dose; reporting at least one renal or cardiovascular outcome.Exclusion: Non-CKD populations; single-arm studies; follow-up below 6 months; studies without extractable outcome data.

Information sources PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, ClinicalTrials.gov, WHO-ICTRP.

Main outcome(s) Composite kidney endpoint (sustained 40% eGFR decline, ESKD, renal death).

Additional outcome(s) eGFR slope (mL/min/1.73m2/year); CV death; HHF; AKI; UACR change; genital mycotic infections; DKA.

Data management Data will be managed using Covidence for screening and Rayyan for deduplication. Extracted data stored in pre-piloted Excel forms. Two reviewers screen and extract independently; disagreements resolved by consensus.

Quality assessment / Risk of bias analysis Cochrane RoB 2.0. GRADE for overall certainty. Pre-specified subgroup analyses graded separately.

Strategy of data synthesis Random-effects DerSimonian-Laird meta-analysis. Pre-specified interaction tests: diabetes status; albuminuria stratum; CKD aetiology; individual agent. IgAN subgroup pooled from trials identifying IgAN participants. Five-year eGFR slope: weighted mean from trials with 5-year data.

Subgroup analysis Diabetes status (T2DM vs non-diabetic); albuminuria stratum (UACR below 30, 30-300, above 300 mg/g); CKD aetiology (diabetic nephropathy, IgAN, hypertensive nephrosclerosis, other); individual SGLT-2 inhibitor agent; baseline eGFR stratum.

Sensitivity analysis Sensitivity analyses excluding pre-specified subgroup analyses; restricting to trials with eGFR below 45 at baseline; restricting to non-diabetic CKD only.

Language restriction No language restriction.

Country(ies) involved Saudi Arabia.

Other relevant information Nephrology; Endocrinology; Clinical Pharmacy; Cardiovascular Pharmacotherapy

Keywords SGLT-2 inhibitor; chronic kidney disease; IgA nephropathy; eGFR; albuminuria; meta-analysis; empagliflozin; dapagliflozin; canagliflozin; renoprotection.

Dissemination plans Submission to a nephrology or general medicine journal; KDIGO guideline update committee notification; open-access.

Contributions of each author

Author 1 - Abdulrahman Alanazi - Conceptualization and design of the systematic review and meta-analysis. Literature search strategy and execution (PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, ClinicalTrials.gov through May 31, 2026). Study selection, data extraction, and risk-of-bias assessment. Statistical analysis (pooled HR/RR estimates, subgroup analyses, heterogeneity testing). Interpretation of clinical and pharmacological findings.
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Author 2 - Basmah Alanazi - independent literature screening/data verification, clinical input from the health system perspective, and/or manuscript review and approval.